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PUBLIC HEALTH BULLETIN No. 41

NOVEMBER, 1910

STUDIES UPON LEPROSY

XII. NOTES ON THE STUDY OF HISTORIES OF LEPERS FROM THE STANDPOINT OF TRANSMISSION

BY

DONALD H. CURRIE

PASSED ASSISTANT SURGEON AND DIRECTOR LEPROSY INVESTIGATION STATION

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PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE

Investigations made in accordance with
the Act of Congress approved
March 3, 1905

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NOTES ON THE STUDY OF HISTORIES OF LEPERS FROM THE STANDPOINT OF TRANSMISSION.

By Donald H. Currie, *Passed Assistant Surgeon and Director Leprosy Investigation Station.*

INTRODUCTION.

The most simple method which is employed for the eradication of most communicable diseases is the removal of the affected member from its healthy fellows.

In the case of certain diseases among the lower animals (glanders, tuberculosis, fowl cholera, etc.) this is effected by killing the diseased animal and destroying its carcass.

In the case of human beings the nearest approach to this method that humanitarian ideals will permit is the complete isolation of the diseased person from his fellows until the course of illness has terminated. When we are dealing with typhus or smallpox, this isolation is comparatively easy to effect, as the separation of the sick from relatives and friends is of short duration; but when we attempt to employ this method in the case of a disease in which, like leprosy, the duration of the illness is for the balance of the individual's life, we meet with the resistance of friends and relatives, who, in many cases, prefer to take a serious risk of contracting the disease themselves rather than to surrender the ill to what they know means lifelong and complete separation.

This is especially true when we are dealing with a people that only partially accept our teachings of the communicability of disease; especially true when the system of isolation appears to them to be unnecessarily complete in character; especially true when we deal with a people whose loyalty to family and race is better developed than any abstract ideals of upholding the law for the ultimate benefit of all.

In our present state of knowledge of leprosy it is difficult to see how we can ever hope to eradicate this disease without some form of isolation. We can not say just how complete such isolation must be to effect the results desired, as we do not know how man contracts the disease, except that he acquires it in some unknown manner, directly or indirectly, from some other person afflicted with it. But as our knowledge of transmission in other diseases has increased, our methods of eradication have, as a rule, not only become more effective, but also more humane, and it is safe to say that leprosy will be no exception to this rule.

Even in our present state of knowledge, certain countries, notably Norway, have developed a system of isolation which, at first sight, hardly appears strict enough to be termed isolation, yet this very country has practically stamped out leprosy by no other measures than the one referred to. On the other hand, in countries like Hawaii, where those apprehended are completely banished, absolute failure to lessen the incidence of the disease has resulted, not because the banishment of *all* cases would not eradicate the disease, but because the isolation is made so complete that the relatives of the afflicted refuse to comply with the spirit of the law and report their sick.

In the case of Norway the cooperation of the people has been secured by instituting a modified form of isolation; in the case of Hawaii the cooperation of the people has not been secured, on account of the absolute character of the isolation.

Just how completely must we isolate a leper from his fellows to make the latters' infection a remote possibility? An exact answer to this question can only be given when we have an exact knowledge of the means whereby we acquire the disease from those afflicted with it.

Now that we can grow the bacillus of leprosy on artificial media we may hope to be able to approach the subject of transmission by a direct method of study. Nevertheless, for the present at least, indirect means of studying the problem will continue to offer hope for its solution.

Of these indirect methods of studies of this problem there are few which offer more promise in illuminating the subject of transmission than that of case study—the study of the histories of lepers for the few years preceding the first symptoms of the disease.

It must be admitted, however, that the value of such evidence depends largely upon the locality. Those places where cases of leprosy are few offer a better opportunity than places where the reverse holds true, for the reason that in the former case, when we can trace a contact, of a certain character, with a leper several years before the disease develops in the patient whose history we are investigating, it becomes reasonably certain that that patient contracted leprosy from the person referred to and during the contact described.

On the other hand, when we obtain a history in a locality so badly afflicted with the disease that the patient knows that he or she has been in contact with a leper two, three, or half a dozen times, we must presume that there have also been many unknown exposures, which makes it impossible to judge just when and by what kind of contact the disease was contracted.

It will be seen by the study of these notes that we are attempting to investigate the disease in one of the least favorable countries for such transmission studies, some of our cases having been exposed intimately, to their knowledge, several times, but even such data have their value.

As to the accuracy of the histories themselves, this is obviously most important in data of this character. We believe that the data we present here are as accurate as the average clinical history obtained elsewhere. None of the data presented here were given until we had thoroughly questioned and in some cases cross-questioned the patient after an interval of several weeks, keeping only those answers which were borne out by the further testimony of the patient.

In this connection it is hardly necessary to point out that when the average patient states that he was in contact with a certain disease at a certain time, even though the patient may be truthful, he may have erred, usually not being an expert diagnostician; but from its frequency Hawaiians have learned to know the symptoms of leprosy fairly well, probably being as familiar with them as the average person of the same class in other countries is familiar with the symptoms of pulmonary tuberculosis.

Another point to be borne in mind when considering these histories is the fear that these patients entertain that evidence of this character may be used to apprehend and isolate relatives and friends, now at large and known to the patient as suffering from leprosy. We have done all in our power to assure them that no such use would be made of such data, but this defect, of course, does not detract from the statements that they *were* exposed to a certain case at a certain time. The only way that it could influence the histories would be to withhold some statement bearing on an exposure, which they feared would be against the interest of some relative or friend.

The following histories were obtained either from patients under our care or from such under the care of the territorial board of health.

Case 1: Patient is about 18 years of age. He does not remember just how long he has had leprosy, but knows that he had the first symptoms before he entered school. At the time that he sickened some ten persons were living with him; three of these people had leprosy at that time. He does not know how long these people had suffered from leprosy, but knows that they had the disease for several years previous to the development of his first symptom. One of these persons is his father, who still lives in Honolulu. The other two are cousins. Both of these cousins have since been isolated. One of them was sent over to the settlement at the time the patient was. After developing the disease, the patient entered a Honolulu boarding school. He did not know of any leper being at this boarding school at that time, except himself. Since patient was isolated, however, one of his former schoolmates has been sent into isolation. This schoolmate not only attended school with patient, but slept in the same bed with him, sat beside him, and often played with him. All of this occurred, as before stated, after "Case 1" knew that he was suffering from the disease.

The first symptoms patient noticed were red spots on his cheeks. Up to the time that he was isolated he never saw a leper that he knows of, except the three persons living in the same house with him. He has brothers and sisters, who are well; no relative other than the two cousins has ever been sent to isolation.

When he entered isolation he found a leper there whom he had known in Honolulu before the former developed leprosy, but there is no history of intimate contact with this case. He has had what he believed to be itch, but only *after* he developed leprosy. He was vaccinated while at school, i. e., *after* he developed leprosy.

Case 2: Patient is 56 years of age; a Hawaiian of intelligence; has had leprosy for the last three years. His first symptoms were red spots on his forehead. He gives the following history of known exposures to the disease: He lived in the house with his father, who had leprosy and died of this disease in 1886. His father suffered from this disease for three (?) years previous to his death, all of which time was spent in the latter's residence in Honolulu.

In 1902 patient was employed as a nurse in Hilo, Hawaii, and for the next four years he nursed a leper in the Hilo Hospital. He developed the disease himself about at the end of this nursing service, and one year later, i. e., 1907, he entered the Kalihi isolation station. None of his relatives were ever sent into isolation. None of the patient's friends were isolated previous to patient being isolated. Some of his friends have been isolated since he entered isolation himself. He had known persons with whom he went to school that were isolated afterwards, but this, of course, was long ago. When serving as a policeman, he sometimes had to arrest lepers. He never was sick with any disease other than this one, never had itch, and was vaccinated fifty years ago.

Case 3: The patient is 18 years of age; he developed leprosy two or three years ago. His first symptom was white spots "all over him." At the time he sickened four persons were living with him; they were all well and have remained so. He never lived in the same house with a leper, but his cousin, a leper, lived 300 yards away from him, and the patient often visited him. Patient's grandmother also had leprosy before he developed leprosy; she lived in the same house with the leper cousin, previously mentioned. The two mentioned relatives have had the disease about six years. His cousin came into isolation with him, but his grandmother was not isolated until last year.

When patient entered isolation he knew no one at Molokai; none of his schoolmates have ever been sent into isolation.

He has had itch, but developed it since he acquired leprosy. He was vaccinated at school nine months before developing the disease.

Case 4: The patient, a European, is 45 years of age. He first noticed difficulty in breathing through his nose. He had no other symptoms except this difficulty in breathing for a period of five years, when eleven years ago spots came out on his body, the first one appearing on his right leg. He was isolated eight years ago, i. e., three years after the spots appeared. He gives the following history of exposures: He lived with a woman who had just previously lived with a man suffering from leprosy. The woman did not develop leprosy; patient lived with this woman for about a year. It was about three years after patient ceased to live with this woman that the nasal symptom appeared. Patient had also worked for a man in Honolulu who had leprosy and who afterwards died in isolation at Kalihi.

Upon cross-examination, patient states that the man who had previously lived with the woman referred to and who was afterwards isolated, lived for some time in the same house with the patient in Honolulu, and they sometimes ate together.

Patient was vaccinated as a child in Europe and again in 1901, i. e., after he had developed leprosy, but a year before he was isolated.

Case 5: Patient is 17 years of age; developed leprosy about seven years ago. He remembers that his first symptom was a "little white spot," but he forgot where it appeared. He has never lived with a leper. None of his relatives have leprosy, and the only history of exposure he gives is that while attending school in Honolulu, when he was 8 years of age, there was a boy in the same class with him, who was shortly afterwards sent to Molokai. This boy sat in the same seat with patient, and, to use the patient's words, "had plenty of sores."

Patient has had itch, but not until after developing leprosy. He was vaccinated when he was small.

Case 6: The patient is only 12 years of age, and, therefore, his history can not be of much value. He does not know how long he has had leprosy. He only knows that his face became red and then white spots appeared on his abdomen and back. Three people were living with him at the time that he sickened, but they have remained healthy. He was isolated three years ago; none of his relatives have ever been lepers that he knows of. The only exposure that he remembers was being taken once to the Kalihi receiving station, presumably to see some friend of his family, who had been isolated. Nothing more definite in the form of a history could be obtained from this child.

Case 7: Patient does not know his exact age, probably about 18 years. Developed leprosy when a child. Remembers seeing first spots on his back and legs. As a child he played with a leper. He knows nothing of his parents.

Patient was isolated nine years ago, but he does not remember how long he was sick previous to his isolation. He never attended school. Patient had an uncle sent into isolation before he could remember and, he believes, before he was born. Patient also had a cousin sent to isolation before he came himself. He never saw this cousin until he saw him at Molokai.

Patient had itch when he was about 7 years old and has also suffered from rheumatism. He has never been vaccinated.

Case 8: Patient is 24 years of age. He developed leprosy eleven years ago. His first symptoms were white spots on his buttocks. At the time that he sickened 14 other persons were living in the house with him, and 3 of these were suffering from leprosy. He was isolated in 1902, i. e., three years after he developed the first symptoms of leprosy.

Patient has a grandfather, uncle, sister, and cousin who have been sent to Molokai with leprosy. He has friends who were sent to Molokai before he was sent, and other friends have been sent over since he was isolated. Some of these persons are former schoolmates of his.

Patient had itch when he was 11 years old, two years before he developed leprosy. He was vaccinated when 14 years old, i. e., about the time or after his first symptoms developed.

Case 9: Patient is 18 years of age. He developed leprosy seven years ago, the first symptoms he noticed being light-red spots in his face. At the time he sickened six other people were living in the house with him. They were healthy and have remained so. He never attended school with a person whom he knew at that time to have leprosy, but from the boarding school he attended one boy was sent into isolation at the same time that the patient was, and another boy from the same institution was sent into isolation after the patient was isolated.

Patient entered isolation three years ago, i. e., four years after developing the disease. He has been vaccinated three times, had itch after he entered isolation, but never before he developed leprosy.

Case 10: Patient is 20 years of age, of European parentage, and lived among good surroundings. He developed leprosy last year and was isolated three months afterwards. The first symptoms he noticed were red spots in his face and numbness of hands.

He never saw a case of leprosy until he developed it himself. He had an uncle who was sent into isolation before the patient was born. Fifteen years before developing the disease the patient played with a boy who afterwards died at Molokai of leprosy. With the exception of the uncle and the boy mentioned, no friend or relative of the patient was known to have leprosy before patient himself developed it, nor have any of his friends or relatives been isolated since the patient entered isolation. Patient sometimes went on fishing expeditions and during these spent nights in the houses of Hawaiians.

Case 11: Patient is 69 years of age, and developed leprosy two years ago, entering isolation a few months later. The first symptoms that he noticed were "spots on his body," swelling of left ear, and numbness in hands. Patient has seen several lepers, but only casually in the streets of Honolulu; knows of no intimate exposure, but his duties were such as to bring him in daily contact with many Hawaiians. He never had any serious illness up to the time he developed this trouble.

Patient never had itch; was vaccinated in 1880. None of his friends or relatives have leprosy.

Case 12: Patient is 32 years of age. He developed leprosy five years ago; entered isolation two years ago. The first symptoms he noticed were a few spots on his back.

None of patient's friends or relatives have ever had leprosy. He never lived with a leper. He has seen lepers on the Island of Hawaii, but did not recognize the disease at that time. Some of his casual acquaintances have since been sent to Molokai, but no history of intimate exposure could be obtained.

Patient never had itch; was vaccinated when a child.

Case 13: Patient is 50 years of age; a well-developed case; states she does not know how long she has had leprosy. She was isolated eight months ago. Up to about the time she sickened she was engaged in the manufacture of poi.

Patient was vaccinated fifteen years ago; never had itch. The patient, before illness, resided in a small village on the island of Molokai, some distance removed from the leper settlement on the same island, and a district that has furnished a considerable number of cases of leprosy.

Case 14: Patient is 20 years of age. She always lived in Honolulu. The first symptom she noticed were red spots "all over her body." Patient claims to have had the disease eleven months, but in this matter she evidently desires to avoid our knowing the facts. She was isolated nine months ago. Her sister died of leprosy in isolation nineteen years ago. Her grandmother and uncle had been sent to Molokai with leprosy. The patient "stayed sometimes at houses where lepers lived," and "knew lepers in the country, but all are now on Molokai:" she also adds that she played with lepers when a child. She did not go to school with a leper that she knows of. Patient's answers regarding lepers she has known are guarded, probably due to the fear that such information might lead to the apprehension of some of her friends, now at large.

Patient has had itch; was vaccinated while at school.

Case 15: The patient is 17 years of age, has had leprosy for seven years, and was isolated three months ago. Two boys with whom he went to school and often played with were sent into isolation before he was. He has "seen people taken to Kalihi with leprosy." He has always lived with his parents in Honolulu. None of his relatives have leprosy.

Patient had itch several times before developing leprosy, and was vaccinated when he was 6 years of age.

Case 16: Patient is 16 years of age, states he became sick three months ago. The first symptom he noticed was the appearance of macules on the face. One of his sisters developed leprosy some years ago and died of it. Patient played with this sister while she was suffering from the disease. Patient has attended a certain Honolulu school; while there one of his schoolmates was sent to Molokai. Besides this sister and schoolmate, patient has seen "several" other lepers at the school he attended. He was vaccinated when small. Never had itch or any illness before developing leprosy.

Case 17: Patient, 14 years of age, developed leprosy eight months ago; first lesions being macules on both legs, posterior aspect.

Patient's brother developed leprosy some time ago and patient played with him while latter was suffering from the disease. Patient's sister is also a leper, developing the disease ten months before the patient did; sister now at the Kalihi receiving station. Patient also has three cousins that are lepers.

She states further that some of her friends have developed the disease and are now also at the Kalihi receiving station. She lived in Kauai and attended school there, but never saw a leper at the school she attended. Has never had any illness previous to developing leprosy. Has never been vaccinated.

Case 18: Patient is 14 years of age, has had leprosy two years. Disease began with macules on legs, just above ankles. Patient only knows of one exposure—and that with some doubt—a girl lived near her in Honolulu that patient thinks was suffering from leprosy. She played with this suspect up to three years ago. All of patient's family are well and she never saw a leper among her schoolmates. Patient has never had itch. She was vaccinated four years ago.

Case 19: Patient is 12 years of age; both he and his brother developed leprosy at the same time, i. e., six months ago. First symptom patient noticed was a macule on left cheek.

He does not know when, if ever, he was exposed to the disease; none of his family have ever suffered from it, that he is aware of. He attended school in Honolulu; none of his schoolmates nor his friends have developed the disease as far as he knows.

Patient has never had itch; he was vaccinated six years ago.

Case 20: Patient is 17 years of age and sister of "case 17." Developed leprosy eighteen months ago. First symptom noticed was a "cold," followed by nodular lesions of left arm. Otherwise her history agrees perfectly with the history given by her sister.

Case 21: Patient is 18 years of age; has had leprosy for three years, the first symptom appearing on the left foot. Patient has one brother and one sister who also developed leprosy some years ago, the former having died of leprosy at Molokai. Also one of the patient's friends developed leprosy some time before the patient himself did.

With the exception of these cases, the patient's statements are somewhat vague.

SUMMARY.

From the data gained in these few histories, the following points are worthy of notice:

First. A large percentage of the cases give a history of exposure to leprosy some time before they themselves developed the disease. Usually such exposures were of an intimate character.

Second. While itch was a common disease among these cases, there appears to be no definite evidence that a connection existed between the occurrence of itch in some of these patients and the subsequent development of leprosy.

Third. There is nothing in these histories to indicate any relationship between vaccination and the spread of leprosy.

A CONTRIBUTION TO THE STUDY OF RAT LEPROSY.

By Donald H. Currie, *Passed Assistant Surgeon and Director, Leprosy Investigation Station*, and Harry T. Hollmann, *Acting Assistant Surgeon, Leprosy Investigation Station, Public Health and Marine-Hospital Service.*

INTRODUCTION.

The close resemblance between the lesions of rat lepra and of human lepra are well known, and for this reason any new observations that are made in the case of the animal disease are also of interest, and possible service, in the study of the analogous human affection.

With this idea before us, we requested Passed Assistant Surgeon McCoy, United States Public Health and Marine-Hospital Service, stationed in San Francisco, to procure for us twelve white rats (*Mus albus*), inoculate them with rat lepra, and forward them to this station. Twelve of these animals were inoculated by him in December, 1909, and reached us several weeks later.

These animals apparently remained in good health from the day of their inoculation (December 7, 1909) up to May, 1910, when several sickened and later died with the lesions to be subsequently described.

Before presenting these observations, however, we shall review the literature of rat leprosy.

LITERATURE BEARING ON RAT LEPROSY.

Stefansky (*a*) made the first recorded observations on this affection. He recognized two forms of the disease, one the "purely glandular" and the other the "skin muscular" ("Hautmuskulär"). The former was the more frequent in his experience.

In the glandular form he met with cases in which one gland alone was affected, the rest of the body being presumably healthy, and in such cases it was generally an axillary gland that was involved.

Stefansky describes the "skin muscular" form in nine cases. From the description it appears that his cases were all far advanced, as large areas were involved, not only of the skin, but also the underlying muscles to a depth of one centimeter. He inoculated other animals without results. These failures apparently were due to not waiting sufficiently long for the results. In one case he noted a collection of pus-like material following intraperitoneal injection.

Rabinovitch (*b*) became familiar with the disease in Odessa from observing the work of Stefansky. She returned to Berlin and searched for the disease among the rats there. She describes two such infected animals. In each she noticed what appears to be an earlier stage of the disease than that seen by Stefansky in Odessa. But the disease was sufficiently advanced, even in Rabinovitch's case, to show numerous scattered lesions of the skin, with some involvement of the lymphatic glands. At the time of writing, i. e., five weeks after the inoculation of her animals, the latter had failed to develop the disease.

Dean (*c*) observed a rat suffering from this disease 11 miles outside of London. The case was apparently well advanced, both skin and muscular tissue being involved over a considerable area. At the time of writing, i. e., fifty-six days after the inoculation of his animals (2 white rats) he had failed to reproduce the disease.

The same author (*d*) states that since writing in 1903 he has observed six more examples of the disease, as it naturally occurs in rats, and also that, since writing his first article, he has succeeded in obtaining a number of positive inoculation results in rats.

Dean believes that there is no very strict line of demarkation between the two types, as described by Stefansky. Dean describes the disease as met with in well-developed cases and also mentions rarer types of late cases, which showed involvement of the liver and lungs. He has found the specific bacilli twice in the nasal secretions, and he has noted mutilations, such as loss of toes and tails.

Dean inoculated 30 rats with the material obtained from his leper rats. In 9 of these 30 rats he was successful in reproducing the disease; in 3 cases he was able to reproduce the disease to the third generation. Death of the inoculated animals occurred from six to twelve months after inoculation.

> * * * Subcutaneous inoculation was in several instances followed by the production of a local lesion, but this was not a constant result. The lesion consisted of a nodule, containing a semicaseous-like substance, resembling the material which was present in the skin infiltration of naturally infected animals. The acid-fast bacilli were very numerous in these local lesions. The lymphatic glands in such cases, even at a distance from the lesion, were sometimes invaded by the bacilli and showed the changes already described.

Several of Dean's rats died of what he believed to be "intercurrent affections," the nature of which he does not state.

Tidswell (*e*) noted the disease in a single animal, captured in Sydney in 1901. Its skin was abundantly studded with nodules; the neighboring glands were not involved.

The "Reports on Plague Investigations in India," issued by the advisory committee appointed by the secretary of state for India, etc., and usually referred to as the "English Plague Commission to

India," (*f*) contain the following note, which is given in full: "It is perhaps worth recording that the leprosy-like disease of rats, due to acid-fast bacilli, described by Stefansky (Centralbl. f. Bakt., vol. 33, 1903, p. 481) and Dean (this Journal, vol. 5, p. 99) has been met with in *Mus decumanus* in Bombay and in *Mus rattus* in the Punjab."

Bull (*g*) has written on this subject, but the original of this article is not accessible to us and neither of the two publications, quoted as referring to it have abstracted the article. His observations are therefore, unfortunately, unknown to us.

Wherry (*h*) wrote an article from his experience with two rats that were suffering from the disease. The animals presented general subcutaneous congestion, congestion and hypertrophy of the cutaneous, axillary and inguinal glands, numerous minute yellowish tubercles in the subcutis and irregular nodular thickening of the skin. Before his article went into press the author adds two more cases of the disease which, however, like the previous ones, were rather far advanced. At the time of writing, i. e., two months after the observation, the two white rats inoculated had not developed the disease. This investigator examined a flea caught from one of the infected animals, but found no acid-fast bacilli in the insect.

The same author (*i*) later shows that certain flies (*Calliphora vomitoria*, *Lucilia Caesar*, *Musca domestica*) will imbibe and discharge the rat lepra bacilli. The only portion of this latter article that bears upon the subject with which we are now dealing are the results of his examination of ecto-parasites of leprous rats. He examined one specimen of *Ceratophillus fasciatus*, one specimen of *Ctenopsyllus musculi*, one rat louse (*Hamatopinus acanthopus*), and one cone-nosed arachnidian, but found no acid-fast bacilli in these parasites. In the same paragraph the author states:

> The character of the early lesion present in naturally acquired cases of this disease seems to point to inoculation through the skin.

It is evident from this that the earliest cases observed by this author showed involvement of the skin.

In 1909 the same author (*k*) states:

> A leper rat (*Mus norvegicus*, male) in a very advanced stage of the disease was seen to be literally covered with louse eggs. Only a few lice could be found. Six of them (*Hæmatopinus spinulosis*) were ground up on a slide and stained for lepra bacilli. Several hundred acid-proof bacilli resembling the bacillus of rat leprosy were found scattered about in what appeared to be the granular contents of the intestinal tract.
>
> These examinations were made in April, 1909, and are the only ones made on rat lice taken from leper rats since the publication of a previous note. A number of lice from normal rats were examined for acid-proof bacilli, with negative results.

McCoy (*l*) states:

> The essential lesion, or at least the one invariably found, has been a more or less general infiltration of the subcutaneous tissues, and the peripheral lymph glands, with an enormous number of fine white or slightly yellowish granules. At times this infiltration forms a general layer covering the whole surface of the body between the skin and muscular tissues. At other times it is more or less patchy in distribution.

He then mentions the glandular involvement, alopecia and ulcerations. Once he met with visceral rat leprosy in an advanced case. At the time of writing he had made a number of inoculations, but sufficient time has not elapsed to show any results from these experiments.

The same author (*m*) again writes from the experience of 8 rats. The article deals with the epidemiology of the disease. The subjects of parasites or early lesions, with which we are now dealing, are not covered.

The editor of the Lancet (*n*) mentions the presence of rat leprosy in San Francisco.

Mezinescu (*o*) describes late cases of rat leprosy observed by him, the animals showing ulcerations of the skin, etc.; rarely he met with visceral lesions.

Walker (*p*) speaks from her experiences with 14 rats which had naturally acquired rat leprosy, and states:

> Of the 14 positive cases all showed alopecia more or less marked in degree—sometimes confined to some one region * * *.

In only 1 case out of the 14 were the glands involved; none showed visceral lesions. Of the 3 animals of which she publishes the necropsy notes 1 appears to have shown rather localized lesions of skin and in 2 the involvement of the skin was quite general. No mention is made of parasites in relation to the disease.

Kitasato (*q*) found four leprous rats in Tokyo. He mentions the alopecia, skin and subcutaneous tissue lesions, and involvement of the glands. The subject of early lesions and insects is not considered.

Brinckerhoff (*r*) after reviewing the literature, records below-mentioned lesions, which he has observed in the experimental disease (the naturally acquired disease never having been noted in the Hawaiian Islands): Slight enlargement of the peripheral lymph nodes, which contained the bacilli; microscopic lesions of the liver containing the bacilli, the negative results from the examinations of the nasal secretions.

To the above literature we desire to add the personal communication from McCoy, informing us that in San Francisco a large percentage of the leprous rats were afflicted with scabies.

In the later months of 1908 the former director of this station, Dr. W. R. Brinckerhoff, had secured some rats from San Francisco that had been artificially inoculated with rat lepra and which later died of this disease. After we had made these observations, to be later described, we remembered Brinckerhoff's previous work and looked up his records. From these we chose the following necropsy notes as having an interesting bearing on the subject. The following are these notes in full; they have not been previously published as such, although the article referred to above under his name (Brinckerhoff) was probably in part based on these autopsies:

UNPUBLISHED NOTES OF BRINCKERHOFF ON WORK WITH RAT LEPROSY.

I.

Rat found dead. Male. Autopsy: Some odor of decomposition. In lower abdomen a tumor mass, 3 by 2 by 2 centimeters, which is a cyst with a wall 2 or 3 millimeters thick, and filled with a yellowish green caseous material. Other abdominal organs appear normal. Lungs hyperæmic and lower right lung shows white nodules, 2 millimeters in extent, which on section contains creamy pus. Smears from material from abdominal tumor shows large number of bacilli with the morphology and staining reaction of bacillus lepræ. Smears from nares negative.

II.

Rat. Full-grown male. Presents open ulcer on abdomen about its center, 2 by 1½ centimeters in extent, with slightly elevated edge. Near center is white nodule, 4 millimeters in extent, forming slight elevation 2 millimeters high on base of ulcer. Base of ulcer smooth, edges smooth and not overhung. Pale white to yellow color. On dissection nodule described incised and smear shows numerous acid-fast bacilli; left axillary lymph node slightly enlarged, 5 millimeters in extent; other peripheral lymph glands not notably enlarged. Internal organs appear normal, smear from spleen negative. Left axillary lymph node and bit of tubercle in base of ulcer ground in sterile mortar with sterile salt solution. Smear of suspension shows many acid-fast bacilli.

III.

Large white rat; hair sparse all over body, no definite areas of alopecia, many fleas. Chlorformed, fleas collected and smears made by crushing abdomens (of insects) * * * smears from fleas negative. Axillary glands and inguinal lymph glands appear normal. Abdominal organs appear normal in the gross. Smears from spleen pulp show moderate number of acid-fast bacilli, usually single, 'some slender, some about the size of a tubercle bacillus. On opening the thorax, the only lung tissues remaining is the left upper lobe, which appears approximately normal. Both lobes of the right lung and the left lower lobe have been converted into abscess cavities, each approximately 1 to 1½ centimeters in extent. On incising these cavities, the contents is a rather dry granular caseous material of grayish color. The caseous material is readily removed from the tumor, leaving a definite thin wall, about 2 millimeters in thickness, with a smooth inner surface. Heart not notable. Smear made from caseous material shows no bacteria.

IV.

This rat appears to have died in the early stage of the disease; necropsy showed a "tumor" of the skin. The following are taken from the necropsy notes:

"Section (of 'tumor') shows a part of the central caseous mass and the wall of the tumor. No definite limiting membrane can be made out. The central mass consists of granular débris, containing masses of slender bacilli, interspersed with small irregular blue staining masses (nuclei débris), and amorphus granular material (necrotic tissue). The bacilli took the Eosin stain; they are distinctly beaded. As one passes from the necrotic central mass outward the tissue elements become distinguishable as elongated cells with oblong or oval vesicular nuclei lying among wide bands of connective tissue substances. The protoplasm of these cells are crammed full of slender, beaded bacilli. Occasional islands of plasma cells are found. From there outward the tissue seems to be composed of large areas of cells with distorted vesicular nuclei whose protoplasm is filled with the bacilli, the cell groups being marked off by bands of relatively normal connective tissue bearing small blood vessels. In this region the picture is strikingly like a human leproma. The bacilli which take the Eosin are also alcohol and acid fast. Lung: In one area the alveoli are filled with coagulated serum, elsewhere are large and small foci in which the bronchi and adjacent alveoli are filled with polynuclear leucocytes. Lung stained with carbo-fuchsin shows no acid-fast bacilli. Process seems to be acute purulent bronchitis with peribronchial pneumonia. Probable cause of death?"

SUMMARY OF THE REVIEW OF LITERATURE OF RAT LEPROSY.

It will be seen from the above abstracts that other observers have noted pulmonary lesions in rat lepra, but they either passed them over without recording any conclusions as to their significance or they considered these pulmonary lesions to be a late lesion of the disease, secondary to the involvement of skin and lymph nodes.

We also see that in the few recorded examinations of the ectoparasites of the leprous rats, previous investigators have failed to discover the rat lepra bacillus in these parasites' bodies, except in the case of Wherry (*k*) who found them in the bodies of the six lice he examined.

INVESTIGATIONS OF WRITERS OF THIS ARTICLE.

The following are the notes recorded by the writers of this article on several cases of rat leprosy that have recently been inoculated by McCoy in San Francisco, in December, 1909, and sent to this station.

It will be observed that we failed in the case of the first few rats to recognize the fact that the pneumonia present was due to the bacillus of rat leprosy, but considered the pneumonia as an accidental lesion.

RAT I.

A full grown white rat which had been inoculated with rat lepra by Passed Assistant Surgeon McCoy in San Francisco on December 7, 1909, was found dead in its cage on May 3, 1910.

The following are the autopsy findings:

Skin normal; shows neither thickening nor ulceration. Alopecia not present. Animal in state of good nutrition. All organs macroscopically normal, except the lungs, both of which show areas of broncho-pneumonia scattered throughout their lobes. A smear was made from the cut surface of the organ and stained for acid-fast bacilli. A short search was made (at that time we did not connect the pulmonary lesion with rat leprosy). It showed no acid-fast bacilli. Cocci, occurring in pairs, were found scattered through the fields, very few in number, but as no other organism was found it was presumed that these were the cause of the animal's pneumonia.

Comment.—From our experience in the rats that died afterwards it is probable that a few acid-fast bacilli would have been found had the search for them been long enough, but inasmuch as we did not think of pneumonia as an *early* lesion of rat leprosy we were satisfied when we found the diplo-coccus and searched no further. During the autopsy a number of mites (*Laelaps echidninus*)[a] were collected, smeared on microscopical slides, and fixed ready for staining. When we failed to find any evidence (that we then recognized) of rat leprosy, the smears from these parasites were unfortunately destroyed without examination. It is interesting to note, however, the fact that these parasites were present in immense numbers on this rodent.

RAT II.

Autopsy.—Animal in good condition; no alopecia observable; abdomen shaven to obtain a better view of the skin. In the medium line, just below a point half way between the sternum and the pubis, is a white V-shaped scar, with its apex pointing toward the pubis, certainly the result of a wound, and probably the point at which the animal was inoculated. Extending from this point toward the pubis is an area of infiltration of the skin, irregular in shape and covering about one-half of a square inch. The area extends toward, but not to the inguinal glands on both sides. The skin covering this area appears to be thickened, but upon closer examination it is found that this is due to infiltration of the subcutaneous tissues, and that the skin when dissected loose shows irregularly scattered areas of atrophic thinning. The subcutaneous tissue at first sight appears like fat and is filled with small white granules; the abdominal muscles lying underneath this area are normal; the inguinal and axillary glands are not involved. The viseeræ are normal, except the lungs, which show a double broncho-pneumonia. Smears made from the lungs show a Gram-staining diplo-coccus in small numbers; another smear from the lung is stained for bacilli lepræ, but an examination of short duration fails to show acid-fast organisms.

The area of infiltrated skin and subcutaneous tissues show large numbers of slim, acid-fast bacilli, very similar to the human lepra bacillus in morphological and tinctorial peculiarities. The inguinal glands show no bacteria of any kind.

The body surface of the animal was found to contain 54 mites (*Laelaps echidninus*). Seventeen of these were killed, mashed, smeared on glass slides, stained with carbo-fuchsin (Nielson), decolorized with 1 per cent nitric acid in 70 per cent alcohol for ten seconds, counterstained with Loeffler's alkaline-methylene blue, and examined under the oil-immersion lens. Of these 17 mites, 4 showed typical rat-lepra bacilli in considerable numbers, these bacilli differing in no respect from those contained in the tissues above described, even to the occurrence of the characteristic clumps. Thirty-two of these parasites were placed on three specimens of rats (*Mus alexandrinus*), no uninoculated white rats being available for this purpose.

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[a] We desire to acknowledge the aid furnished us by Messrs. Nathan Banks and David T. Fullaway, United States Department of Agriculture, who kindly identified this parasite for us.

One hundred house flies were fed with the leprous infiltrated subcutaneous tissue, placed in a cage with two other roof rats (*Mus alexandrinus*) whose tails had been abraded by scraping, so as to make them attractive to the flies and also to afford a lesion for the possible entrance of the bacilli.[a]

The remaining 5 ecto-parasites were reserved for species diagnosis.

We excised several pieces of lung tissue and placed them on glycerin agar slants. These latter were incubated at 35° C. to 37° C.

RAT III.

Autopsy notes.—Skin and subcutaneous tissues perfectly normal. All viscera normal, except lungs, which show the same broncho-pneumonia noted in the first two animals. Examination of these lungs showed a few diplo-cocci, after long search, hardly sufficient to consider them infecting agents, but no other bacteria were demonstrable by the ordinary anilin stain, and a short search after the staining for acid-fast bacilli with carbo-fuchsin, acid alcohol, alkaline-methylene blue, counter stain, showed no acid-fast bacilli. Autopsy was closed without satisfactory explanation having been obtained as to the cause of the animal's death.

RAT IV.

Found dead on May 10. Autopsy shows neither ulceration of skin nor alopecia. The skin, subcutaneous tissues, superficial muscles, and lymph nodes normal.

All viscera normal, except the lungs, which showed a broncho-pneumonia with small abscesses scattered throughout the pneumonic areas.

Four mites (*Laelaps echidninus*) were captured from the body of this animal. These parasites were crushed and smeared and these preparations stained for acid-fast bacilli.

The lungs were placed in sterile dishes for further examination; the other organs of the animal appearing normal, the animal (except its lungs) was destroyed. A few hours later the lungs were incised through under aseptic precautions, a number of smears made from them and stained for acid-fast bacilli. Careful and prolonged examination of these smears were made with the result that an immense number of acid-fast bacilli were observed, these bacilli, however, were not evenly distributed through the lung substance, long search often failed to show any in some of the smears, but when found at all, they were present in clumps containing great numbers. They were slim, acid-fast rods, occurring singly and in clumps, and were in every way typical of the bacillus of rat leprosy.

We then examined the smears from the four mites. Two of these parasites showed typical rat lepra bacilli in considerable numbers. Two showed no lepra bacilli. In the previous rat (Rat II), when we found the bacilli in these parasites, we supposed they had imbibed them by feeding over the skin lesion of that rodent. But this rodent (Rat IV) had no skin lesion, so the presence of the lepra bacilli in these mites would appear to indicate that a septicemia existed. As the body of the rat had been destroyed, we could not confirm this. After finding the acid fast bacilli in the lung of this rat, we returned to Rat II and removed a small portion of the lung tissues of that animal, that we had placed on the glycerin-agar tubes (*vide supra*). Examination of this lung tissue showed an immense number (it was estimated an average of 2,000 to 3,000 lepra bacilli per oil immersion field) of typical lepra bacilli; every field being crowded with them. Considering the negative results of the first examination of these tissues when fresh, it was not possible to believe otherwise than that these bacilli had greatly multiplied in the dead lung tissues. No growth, however, had occurred on the surface of the glycerin-agar slants, upon which these bits of tissue had rested. An occasional nonacid-fast coccus was also found, but very few in comparison to the acid-fast bacilli.

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[a] The results of these attempts to inoculate will be reported on later.

From the lungs of Rat IV we inoculated all ordinary laboratory media, including glycerin-agar and glycerin-glucose-agar slants and placed them at 37° C. From these same lungs, containing the acid-fast bacilli, we prepared a heavy suspension and injected 1 cc. of this into the peritoneal cavity of a suckling guinea pig.

From the lung tissue of Rat II that had laid on the glycerin-agar slants and in which so many lepra bacilli were found, we prepared a suspension and injected 1 cc. of it into the peritoneum of another suckling guinea pig.

RAT V.

Autopsy and notes.—After the experience above noted, we chose one of these rats, which had been inoculated with rat leprosy on December 7, 1909, and which appeared to be in perfect health. This animal was chloroformed and a complete necropsy performed, the notes of which appear below:

Careful inspection revealed no lesion of the skin, alopecia, etc. The animal was skinned, but neither skin nor subcutaneous tissues showed any pathological changes of any organs, except a double broncho-pneumonia, involving over one-half of the total lung tissue. Small portions of these consolidated lobes were excised and smeared on a slide, after which they were stained in the usual manner or lepra bacillia. Examination of these smears showed from 3 to 200 acid-fast bacilli per field, these organisms were identical in appearance to the bacillus of rat leprosy.

Smears were made from the heart blood, stained and examined, and a few lepra bacilli were found. Two cultures were taken from the heart blood on glycerin-glucose agar. Another smear was made from the heart blood, fixed with wood alcohol and stained in the usual manner. It showed a moderate number of acid-fast bacilli, varying from one bacillus in ten fields to three bacilli in a single field.

The spleen presented nothing abnormal. It was cut through the central portion under aseptic precautions and a smear made from the splenic pulp, stained, and examined. Examination of this smear showed a few (an average of one organism to three fields) acid-fast bacilli, morphologically identical to the other bacilli noted.

The liver was next examined under aseptic precautions and showed macroscopically no changes. A smear was made from it and stained in the usual manner. Rather prolonged search failed to show any lepra bacilli.

Examination of 11 mites (*Lælaps eschidninus*) showed 6 containing lepra bacilli and 5 not containing lepra bacilli. The examination of 1 louse (not classified) showed 2 lepra bacilli.

Four guinea pigs and two rabbits were inoculated with a suspension of the consolidated portion of the lung.

An uninoculated specimen of *Mus alexandrinus* was chosen and its lungs removed, which, as would be expected, were perfectly normal. It was cut up into small pieces and placed in a Petri dish, after which purulent matter from the lung of Rat V was picked up with a platinum loop and smeared over this bit of lung tissue; in other words, the cut surface of the healthy rat's lung was used as a culture media. The bottom of this Petri dish, containing these inoculated specimens, was moistened with ordinary bouillon to prevent its drying out. Ordinary laboratory media, including glycerin-agar, were also inoculated with the purulent matter of the lung, a portion of the spleen, and heart blood. Some cultures were incubated under aerobic and some under anaerobic conditions.

ILLNESS OF ALL REMAINING RATS.

Soon after this necropsy, in the latter part of May, all of the remaining rats became ill, the most notable symptom being rapidity of respiration and stupor. On June 2 all of the remaining animals (seven) had greatly improved or recovered from this dyspnœa except two.

One of these animals was still very ill on July 11, although its dyspnœa was less marked than at the onset. A description of this animal's condition is given under "Rat VII." The other one of these two very sick animals died on June 13. The following are the necropsy notes on this latter animal:

RAT VI.

Animal sickened in May and became much worse about June 7, with very rapid respiration. It continued in this condition until June 13, when it died. At the time the animal was brought into the morgue its body was found to be swarming with the same kind of mites (*Lælaps echidninus*) noticed in the other animals.

Of these parasites, 34 were captured, their bodies smeared on glass slides, stained with carbo-fuchsin, and examined. All of these 34 parasites showed acid-fast bacilli in at least one-half of the microscopical fields examined. In those fields where bacilli were found in greatest numbers a count was made, which showed the following numbers of bacilli present per field: One field showed 5 bacilli, another field 10, another 17, another 20, another 50, and one showed a clump of over 300 acid-fast bacilli. On the other hand, from 1 to 3 bacilli were the common numbers met with.

Animal was stretched, skin inspected, alopecia and thinning of the skin present over the lower portion of the animal's abdomen. A brawny, fat-like layer is encountered underneath the skin, the examination of which shows myriads of acid-fast bacilli. There is no involvement of the inguinal glands. The same fatty-looking material is encountered around the axillary region, and the right axillary gland is slightly enlarged. It is excised for examination and shows an immense number of acid-fast bacilli. The left axillary gland shows a similar slight degree of enlargement.

The abdominal cavity is opened. The omentum is excessively rich in fat, the spleen is incased in a "sugar-coated" capsule, due to a chronic perisplenitis. The kidneys are surrounded by fat; they are excised for examination.

The thorax is next opened. The organs lie in about normal position. The heart cavity is opened after burning the surface of the organ, and a drop of blood taken, smeared on a slide, fixed, stained for acid-fast bacilli. Lungs are removed. Right lung does not collapse completely; most of the organ is of a light pinkish color, especially the lower lobe, with ivory-white spots scattered over its surface. The upper portion of the lung is dark red in color, except for the white spots mentioned. This portion does not contain the pinkish colored areas seen in the lower lobe. The dark portion of the lung collapses more completely. It is softer to the forceps' touch, the lower being more firm. The left lung is of a uniformly dark red color, but collapses almost completely.

Incision is made into the right lung, lower lobe. Its cut surface presents a white-colored area, showing consolidation. Pressure on this white area causes a cheesy-like mass to exude. Smears made from this cheesy mass, stained with carbo-fuchsin, and examined. Incision through white spots shows that they represent abscesses filled with cheesy matter.

A portion of the spleen is next removed and is found to be incased in a much-thickened capsule, which has a granular white appearance, but is not suggestive of tuberculosis. A smear is made from this spleenic capsule and from the spleenic pulp and examined. Cultures are made from spleen and lung on ordinary media, including glycerin agar.

The omentum is greatly enlarged, fills and distends the peritoneal cavity; a smear is made from it and stained for acid-fast bacilli. This enlargement is due to a fat-like substance, which closely resembles the description given by previous observers of the rat leprous infiltration.

Examination of smears: Smears made from the infiltrated subcutaneous tissues, the heart blood, the lungs, spleen, omentum, all show acid-fast bacilli. The smears from the infiltrated subcutaneous tissues, lungs, spleen, and omentum show *immense* numbers of the bacilli, while the heart blood shows fewer bacilli. The lungs of this animal appear to have been infected for a longer period than the lungs of the other animals examined, and it was believed at the time of necropsy that the appearance of these organs suggested that resolution was taking place in the pneumonic areas and that had the animal lived longer only the small areas of focal necrosis (abscesses) would have remained; but of this we could not, of course, be absolutely certain.

Two guinea pigs, each 6 weeks of age, were inoculated intraperitoneally with 1 cc. each of a heavy suspension of the rubbed-up lung tissue and the infiltrated subcutaneous tissues, these suspensions being very rich in acid-fast bacilli.

RAT VII.

On June 2, among the remaining inoculated white rats, one was noticed to be suffering very severely from dyspnœa, the animal's respiration being two or three times as rapid as normal. From the appearance of the animal we expected it to die in a few days. Inspection made at this time showed no alopecia, ulceration of the skin, nor nodule deposit. The animal was separated from the others and observed. After several days the animal appeared somewhat improved. It frequently came out of its nest to take food, although it seemed to be very weak. The hair of the animal remained normal up to very recently.

Inspection on July 11 shows the following: The animal's respiration is still rapid, but not nearly as rapid as the time it first sickened. It is barely able to crawl around its cage to procure food. Two areas of alopecia have appeared upon its back, the hair is roughed up, but no ulcers are noted. One of the notable features in this animal, as well as in the ones previously autopsied, is the presence of numerous mites (*Laelaps echidninus*), the hair simply being a swarming mass of these parasites, and on the head alone it is not unusual to see 12 or 15 at one time. No lice or fleas were observed on inspection. The animal is being held for further observations.

July 12: Inspection of the remaining five inoculated rats (not including Rat VII) made to-day. Loss of weight, alopecia, and great weakness are noticeable symptoms in several of them. No dyspnœa is noted, although these animals suffered from that symptom in the latter part of last May.

Necropsy notes on rat VII.—Animal has since the last notes been resting quieter and appears to have almost recovered from the dyspnœa, with which it had been suffering for several weeks past, but on the other hand the animal has lost considerable weight. It died on the night of August 9, and was autopsied about 10.30 a. m. the following day. Body very much emaciated; no alopecia present, except the areas mentioned in its clinical history, and one a little larger than the size of a pea, over the abdominal surface. This latter may represent the place of inoculation.

With the exception of these, the skin, subcutaneous tissues, and all the superficial glands are normal.

Abdomen opened. All the abdominal viscera are macroscopically normal.

Thoracic cavity opened. Left lung pale in color. Does not completely collapse, but extends over to the right side of the cavity for a distance of fully 1½ centimeters. This left lung is removed. A number of incisions are made into organ. The larger bronchi and connecting cavities are filled with a cheesy mass, which forms castlike plugs. With the exception of the cheesy matter filling the bronchi and an emphysema, there is nothing abnormal about the organ. No nodules are noted.

Right lung. Organ dark red in color. It is excised. Incision shows numerous hard areas scattered throughout the organ. These areas are found to be filled with the same cheesy matter which fills the distended bronchi and abscesslike cavities of its fellows.

RESULTS OF INOCULATION OF ANIMALS.

All of the animals inoculated from these rats apparently remained in good health. On July 11 they were all chloroformed (from the twenty-eighth to the fifty-fifth day after inoculation). The following are the necropsy notes on these inoculated animals:

ANIMALS INOCULATED FROM RAT V.

The two rabbits and four guinea pigs, inoculated from the lung of rat V, on May 16, 1910, were chloroformed on July 11. These animals have apparently remained perfectly healthy since the day of inoculation; their appetites have been normal and there has been no appreciable loss of weight.

First rabbit.—Large brown rabbit. Autopsy shows a perfectly normal, well-nourished animal.

Second rabbit.—Large white rabbit. Nutrition normal. All organs normal.

First guinea pig.—Medium-sized guinea pig, animal well nourished. The animal was inoculated subcutaneously over center of abdomen, lower half. If we were dealing with tubercle, its first tubercular infection should have occurred in the inguinal glands. These glands, however, are found to be perfectly normal, hardly being visible. The axillary glands are also normal. Thorax opened, lungs and pleura found to be normal, except the spleen, which presents, near its surface, three nodules of the size of a pea, of white color; they are very soft on palpation.

These nodules were incised; they cut easily; a very liquid pus exudes from them. Repeated smears were made from them, stained with carbo-fuchsin, decolorized in acid alcohol and counterstained with Loeffler's methylene blue and thoroughly examined. Examination does not show a single acid-fast bacillus in any of the slides made. A few short, plump, blue-staining rods, occurring in pairs, are found, but in such small numbers as to cause us to suspect them to be accidental or post mortem invaders. The examination is sufficient to show that either the animal has had tuberculosis and has recovered, which is unlikely, or these splenic abscesses are due to some other undiscovered cause. A thorough search is made for secondary nodules of small size throughout the body, but without discovering any. The nutrition of the animal, as previously mentioned, is exceptionally good.

Second guinea pig.—The animal was inoculated at the same time as the previous one, and from the same rat lung. Nutrition and muscular development excellent. This animal was inoculated subcutaneously, like the other pig. Inguinal glands normal in size, incased in fat.

Thorax opened: Heart, lungs, and pleura normal.

Abdomen opened: Unusual amount of mesenteric fat, but not of a character ordinarily met with in rat leprosy. All organs normal. Smears made from the superficial glands nearest to the site of inoculation, stained in the usual manner for acid-fast, bacilli and examined. No bacteria of any kind noted.

Third guinea pig.—Guinea pig inoculated from the lung of Rat V on May 16 is autopsied. Animal shows unusually good nutrition and muscular development. Inguinal glands heavily incased in fat; glands themselves normal.

Thorax opened: Lungs, heart, and pleura normal.

Abdominal cavity opened: Abdominal fat well preserved. All organs, including spleen, perfectly normal.

Fourth guinea pig.—Guinea pig, inoculated on the same day from lung of Rat V, is autopsied. Muscular development and nutrition well preserved. Inguinal glands heavily incased in fat, very minute in size, and normal in appearance. Axillary glands normal in size and appearance, heavily incased in fat.

Thoracic and abdominal cavities opened: Lungs, heart, and pleura perfectly normal. Abdominal fat well preserved. All abdominal organs normal.

ANIMALS INOCULATED FROM RATS II AND IV.

A suckling guinea pig, about 3 weeks of age, was inoculated with an emulsion, formed by rubbing up a piece of the lung of Rat II. Another animal of the same age was inoculated with an emulsion of Rat IV, which was rich in acid-fast bacilli, believed to be bacilli of rat lepra. Both of these pigs received 1 cc. intraperitoneally of this suspension. This method of inoculation was used in order to rule out the possibility of a strain of tubercle that was weakly infective for guinea pigs, it being believed that these tests alone would suffice, the dose being so heavy and the animals being so young. The two animals were placed into a cage with their mother, which latter was not inoculated.

Autopsy notes on suckling guinea pig No. 1 (inoculated from Rat II).—Animal well nourished and muscular development good. Subcutaneous fat well preserved or a young animal. Inguinal glands barely large enough to be visible and encased in fat.

Thorax and abdominal cavity opened, lungs, heart, and abdominal organs perfectly normal. Peritoneum thoroughly inspected, especially about site of inoculation, and found to be absolutely normal.

Autopsy notes on suckling guinea pig No. 2 (inoculated from Rat II).—Size, nutrition, and muscular development exactly like animal just autopsied. Subcutaneous fat well preserved for animal of this age, encasing normal inguinal and axillary glands.

Thorax and abdominal cavity opened. Lungs and heart normal in appearance. Peritoneum, especially about the site of infection, thoroughly inspected for tubercle deposits. The peritoneum, spleen, and other abdominal organs are perfectly normal. The autopsy on these two animals indicates very positively that the emulsion injected into them did not contain tubercle bacilli.

ANIMALS INOCULATED FROM RAT VII.

Two guinea pigs, about 6 weeks old, were inoculated on June 13 from the lung and subcutaneous tissue infiltration of Rat VI. This material was rubbed up into an emulsion. The emulsion was examined and found to be rich in acid-fast bacilli. Each of these animals received 1 cc. They were autopsied on July 11;

i. e., nearly one month from the day of inoculation. The development and nutrition of one of these animals had never been very good, but possibly this is due to its mother deserting it early, as it sometimes happened with our pigs. It has, however, fed well and appeared in perfect health. The other animal was well developed and well nourished and, like the other pig, has always had a good appetite.

Autopsy notes on the first guinea pig of Rat VI.—This is the animal last described as being the one well developed and well nourished. The inguinal glands are encased in fat and of such size as to be barely visible to the naked eye. A slight scar is present in the anterior abdominal wall, at the site of inoculation. The peritoneal cavity is first opened and inspected for nodules or other evidences of tubercular infection, but without results, the peritoneum throughout being perfectly normal in appearance. The spleen and other abdominal organs are also perfectly normal, the peritoneal fat is well preserved. The scar mentioned was probably due to an injury inflicted by the instrument's insertion. The lungs, pleura, and heart are perfectly normal in appearance.

Autopsy notes on the second guinea pig of Rat VI.—This is the one of poor nutrition, probably due to an accident in rearing. Subcutaneous fat is not well preserved. Has very little fat about inguinal and axillary glands.

Thorax opened: Heart, lung, and pleura normal.

Abdominal cavity opened: All the abdominal organs are perfectly normal.

A smear made from the peritoneum of the first of these two guinea pigs is examined and found to be negative as to acid-fast bacilli.

RAT VIII.

Animal found dead in its cage about 5 p. m., July 16. Autopsy was begun on it about two hours later. This animal is one of the rats that sickened in May, when it was noticed to be suffering from rapid respiration, similar to, but milder than the symptoms of the rats which have previously succumbed.

Inspection of the body showed an immense number of mites (*Lælaps echidninus*) crawling over it. These parasites were chloroformed, collected, and counted, and it was found that there were 352 of these mites on the animal's body. Forty-eight of these parasites were chosen, their bodies smeared on glass slides, and examined, with the following results:

Forty-eight mites were examined, 30 fields being examined in each mite.
Three mites showed an average of 2 acid-fast bacilli per mite.
Seven mites showed an average of 6 acid-fast bacilli per mite.
Seven mites showed an average of 8 acid-fast bacilli per mite.
One mite showed 10 acid-fast bacilli.
Four mites showed an average of 2 acid-fast bacilli per oil-immersion field.
Six mites showed an average of 3 acid-fast bacilli per oil-immersion field.
Two mites showed an average of 6 acid-fast bacilli per oil-immersion field.
One mite showed an average of 10 acid-fast bacilli per oil-immersion field.
Two mites showed an average of 20 acid-fast bacilli per oil-immersion field.
One mite showed an average of 50 acid-fast bacilli per oil-immersion field.
Fourteen mites showed no acid-fast bacilli.

Inspection of the animal's body shows the animal to be greatly emaciated. Over its back several areas of alopecia, varying in size from 1 to 1½ centimeters in diameter, roughly circular in shape, are noted. The lower two-thirds of the abdominal surface shows alopecia. This area is only broken by small scattered patches of hair. Two ulcers are noted on the abdomen of the animal, the larger of which is three quarters of a centimeter in diameter, scooped out, edges sharp, not undermined, and base formed by the subcutaneous tissue. The skin in this abdominal area that shows alopecia is infiltrated, or at least the subcutaneous tissues are, and, by their bulging forward, have the appearance of skin nodules. This infiltration is unevenly distributed and has the appearance of fat, but is more granular. A smear is made from this fatty-like substance for microscopical examination, which shows many hundred acid-fast bacilli. There is more congestion of the blood vessels in the inguinal areas than under the skin of the rest of the abdomen, but no enlargement nor other pathological changes are noted in the inguinal glands. The axillary glands are also normal in appearance.

The abdominal cavity is opened. Previous to opening this cavity it is noticed that there is a bulging of its anterior wall. Upon opening the abdominal cavity it is found that this bulging is due to the fatty-like substance deposited in the omentum and to the large size of the spleen, which is also encased in this fatty-like material. This latter organ measured 7½ centimeters in length, 2¼ centimeters in breadth, and nearly 1 centimeter in thickness, and is easily five times the normal size of the spleen of a rat. The weight of this organ is 7.3 grams. Incision is made through this organ, and it is found that this fatty-like appearance is not confined to the capsules, but that the whole organ has the appearance of a piece of tallow, with here and there a small red spot, indicating where the larger vessels are severed. There is no demarkation between the pulp of the organ and the capsule. Three smears are made from the cut surface of this organ for microscopical examination, and many hundreds of acid-fast bacilli were found in each field of the three slides examined.[a]

The liver is next examined. This organ is found to be considerably enlarged, extending far below the center of the abdomen and has the same whitish, tallow-like appearance noticed in the spleen. It cuts with a slight grade, is rather firm. Its cut surface is similar in appearance to the cut surface of the spleen, having the whitish, tallow-like look throughout the organ. Two slides are made from this organ, the microscopical examination of which reveals an average of 50 to 100 acid-fast bacilli per field. The intestines appear normal, except for a hemorrhage, which has filled a portion of the small intestines with blood. The kidneys are normal in size and appearance.

The thorax is next opened. Lungs collapse completely; organ removed is found to be quite normal in size and appearance, except for an edema, probably terminal in character. The color of the organ is darker than normal. Several sections were made through the organ, but the most critical examination could not elicit anything but an edema. As a matter of routine, two smears are made from the cut surface of the lung for examination, which results in the finding of at least 50 acid-fast bacilli per oil immersion field.

In the median line, posteriorily and in the upper portion of the thorax, is located a large tumor, examination of which shows that it is an immensely enlarged mediastinal gland. It is removed and found to be quite firm in character and white in color. It is a trifle over 2 centimeters in length and a little over 1 centimeter in breadth. The thickness can not be accurately ascertained, but it is less than one-half centimeter. Nothing now existing in the lung accounts for this condition in this gland, and it is therefore probable that a pneumonia has existed in the animal, from which it recovered, especially as this corresponds to the animal's symptoms in May. Smears are made from the cut surface of this gland for microscopical examination, which shows many hundreds of acid-fast bacilli per oil immersion field.

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[a] Sections of this organ were stained with hematoxylin and eosin and examined; there is found to be dilatation of the blood vessels, round-cell infiltration, and areas of coagulation necrosis.

Comment.—From the known clinical symptoms of this animal, which afterwards improved, only to later develop alopecia and infiltration of the skin, together with the autopsy findings, indicates that this animal suffered from pneumonia in May last, from which it recovered, the only evidence of the pneumonia remaining at autopsy being the enlarged mediastinal gland.

RAT IX.

This animal was one of those that were suffering, as previously mentioned, in May, from dyspnœa and other symptoms, exactly like those symptoms from which the rats that died had suffered. This animal recovered from these pneumonic symptoms and was apparently well for a time, when it developed alopecia. The only other symptom noticed was that these four rats, of which this is one., were quieter than normal and that their hair presented a ruffled appearance.

Animal was chloroformed on August 11 and body examined. Area of alopecia, 8 to 9 centimeters square, was found over the skin of the back, just above the root of the tail; this area was irregular in shape, extending laterally to the right, on the flank of the animal. The abdomen showed no large area of alopecia, but there was a patchy loss of hair over the whole abdominal surface. No nodules could be discovered on palpating the skin of the animal. No ulcerations were noted. Animal skinned; the whole lower inner surface of the abdomen shows a fatty-like infiltration of the subcutaneous tissues. Except for the amount of it, it would be impossible to say that it was not normal fat. A smear made from it and stained showed immense numbers of rat lepra bacilli, showing that this was a rat leprous infiltration and not true fat. Under the area of alopecia is another such infiltration. Except in the areas mentioned, the subcutaneous tissue of the animal is perfectly normal; neither inguinal nor axillary glands are enlarged.

Omentum found to be loaded with fat. Intestines encased in fat, as are the kidneys. The amount and appearance of this fat-like substance, judging from our previous experience, indicated that this was a part of the disease rather than true fat from excessive nutrition. Smears were made from the omental fat-like substance, which was found to be almost pure oil, and for this reason could only be fixed with difficulty to the slide. Repeated attempts fail to stain bacilli in the smears from this material. It was thought possible that the excess of oil prevented the organism from taking the stain, but a drop of the fluid, examined under low light, failed to show bacilli floating in such fluid.

The spleen appears perfectly normal, as does the liver and the kidneys, and smears made from the spleen show only one rat lepra bacillus to five oil immersion fields, on an average. Thoracic cavity is next opened; lungs appear perfectly normal, no enlargement of the mediastinal glands. Smears made from the lungs, stained in the ordinary manner, show no rat lepra bacilli. Heart opened. Smear made from the heart blood, stained in the usual manner and examined, with the result that no rat lepra bacilli were found.

Five mites (*Lælaps echidninus*) were captured from the skin of this animal, these representing all the parasites present on this animal, which is rather remarkable in comparison to our experience with some of the other rats. Of these five parasites, four were blood-filled; their bodies were crushed and stained in the usual manner, but no rat lepra bacilli were present.

Comment.—The clinical symptoms of this animal and the necropsy findings in the case of its fellows that died of the same symptoms, forces us to conclude that this animal, like its fellows, sickened in May from rat leprous pneumonia; that it recovered from this condition; that there later developed typical rat lepra of the subcutaneous tissues. Attention is called to the absence of septicæmia in this animal at the time of necropsy, and therefore the absence of rat lepra bacilli in the mites feeding on the animal.

Seven healthy white rats were inoculated on August 11, 1910, from the subcutaneous tissues of Rat IX, inoculating them by the subcutaneous method at the root of tail.

RAT X.

The clinical symptoms and subsequent course in this rat were practically identical with those of Rat IX, the only observable difference during the life of the animal being that the alopecia was scattered more over the body, being of a patchy character and showing no large areas of involvement.

Animal chloroformed on August 11. Body examined and it is found that these numerous small areas of alopecia also show excoriation of the skin, which lesions are covered by a crust. The animal is skinned, the subcutaneous tissue from the pubis to the junction of thorax and neck, over the whole abdominal surface, is one mass of leprous infiltration. The flanks and back, however, show no such lesions. None of the superficial lymph nodes are involved. The subcutaneous tissue infiltration is, like in the case of the rat just autopsied, fat-like in character, but of more granular appearance, and with a little more tendency to a pinkish color than in Rat IX. Smear made from this substance and stained in the usual manner showed an immense number of rat lepra bacilli.

Testes dissected and found to be incased in a fat-like material. The right testicle is excised under aseptic precautions. Smear made from the cut surface of this testicle shows an average of three to four rat lepra bacilli per microscopical field, one field showing a clump of 20 bacilli.

Abdominal cavity opened; all abdominal organs macroscopically normal. Considerable fat-like material encasing both kidneys, which substance follows down the course of the ureters. Smears made from it are found to consist only of fluid fat, which refuses to take the stain. Examined fresh specimens, but found nothing resembling bacilli floating in this oily material.

Thoracic cavity opened: Heart and blood perfectly normal, no enlargement of the mediastinal glands. Smears made from the viscera and heart blood are negative as to acid-fast bacilli, except the spleen, which contained an average of 1 bacillus per 15 microscopical fields.

Eight mites (*Lælaps echidninus*) were captured from this animal. They were smeared, stained, and examined, but showed no rat lepra bacilli.

Comment.—The conclusions we reach in this rat are the same as those in the case of Rat IX.

Eight healthy white rats were inoculated on August 11, 1910, from the subcutaneous tissues of Rat X, inoculating them by the subcutaneous method of root of tail.

RAT XI.

This animal, like Rats IX and X, sickened in May with pneumonic symptoms, similar to the others, recovered from these symptoms, and at the present time appears to be in perfectly good health, except that the hair is a little roughened up and shows a slight thinning, but no distinct alopecia.

The animal is chloroformed and skinned. Greater portion of the abdominal area shows typical rat leprous infiltration of the subcutaneous tissues, a smear of which shows many rat lepra bacilli.

Abdominal cavity opened. Intestines incased in this fatty-like material, which is also deposited in the omentum about kidneys and spleen. Spleen itself is normal in appearance, as is the liver and other abdominal viscera. Smear made from the spleen shows no rat lepra bacilli.

Thorax opened: Lungs perfectly normal in appearance, no enlargement of mediastinal glands. Heart cavity opened. Smear made from heart blood and cut surface of lung show no rat lepra bacilli.

Nine mites (*Lalaps echidninus*) were captured from this animal, smeared, stained, and examined, but found to contain no rat lepra bacilli.

RAT XII.

This, like the other animals just recorded, is one of those that in May showed pneumonic symptoms, consisting of accelerated respiration, weakness, etc. Since then respiration has been normal, there being no noticeable symptoms of any kind, except a slowly developing patch of alopecia at the root of the tail. At the time of necropsy this was about the size of a 25-cent piece and absolute in character. Several small patches were also found scattered over the abdominal surface.

Subcutaneous tissues over abdominal surface are infiltrated, right axillary gland is found to be enlarged to three times its normal size. Smears made from the subcutaneous tissue and gland show large numbers of the bacilli of rat leprosy.

Abdominal cavity opened: Spleen and liver appear normal. Smear made from spleen shows no rat lepra bacilli.

Thoracic cavity opened: Lungs appear normal, except the right lung, which shows three small areas of a rough triangular shape near its base, each area being about the size of one-half of a pea. These are deeply red in color, thrown into water they sink. The shape and color suggest that they may be infarcts, but a positive opinion can not be formed until histological studies have been made. Smears made show from one to five rat lepra bacilli.

Histological examination: One specimen is stained with Van Gieson's connective tissue stain and another with hematoxylin and eosin. Walls of bronchi much thickened, this thickening due in part to swelling of bronchial mucosa, but chiefly to an increase in the connective tissue sheath around bronchi. The walls surrounding the air sacs are greatly thickened, and these walls take Van Gieson's stain deeply. Air sacs filled with leucocytes; but little fibrin present. Blood vessels dilated. Diagnosis: Pneumonia with interstitial increase.

CULTURAL ATTEMPTS.

All the cultures on ordinary media, including glycerine-agar and glycerine-glucose agar remained sterile so far as acid-fast bacilli were concerned. We attempted to cultivate the rat lepra bacillus by the method first successfully employed by Clegg for cultivating the human lepra bacillus (and confirmed by Currie, Brinckerhoff, and Hollmann). At the present writing we are not able to report any success in these culture attempts in the case of the bacillus of rat leprosy, but we will carry this work on and report again later.

DISCUSSION.

It is recognized that in the case of these 12 rats we may have been dealing with an example of an unusual mode of onset of this disease. It is also recognized that these animals were inoculated artificially by the subcutaneous method and that under natural conditions this disease may have an entirely different mode of onset. We shall therefore not presume to generalize or point out the possible significance of these observations, but will confine our conclusions to the cases of the above-described animals and hope to present further data on this subject at some future date.

CONCLUSIONS.

The conclusions which we draw from these 12 rats are as follows:

I. In some cases of artificially acquired rat leprosy the onset is with broncho-pneumonia, accompanied by a septicæmia and without other demonstrable lesions.

II. In other cases of this disease pneumonia is a very early lesion, but we can not positively state that it is always the first lesion.

III. That the animal may die in the pneumonic stage before other lesions present themselves or it may develop pneumonic symptoms and recover from the same only to later develop the well-known lesions of chronic rat leprosy; or, again, the pneumonia may persist until after the development of the lesions of the skin and abdominal visceræ.

IV. That during the stage of the disease in which the animal is very ill certain mites (*Lœlaps echidninus*) were found to be very numerous on the animals' bodies.

V. That during the stage of the disease in which septicæmia is marked these mites' digestive tracts contain the bacilli of rat leprosy in considerable numbers, and therefore these parasites may be one means of transmitting the disease. This latter probability, however, is, of course, not proven.

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